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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,640	12/20/2004	Masayuki Furuya	1034232-000029	2846

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EXAMINER	
KRISHNAN, GANAPATHY	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
08/15/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/518,640	**Applicant(s)** FURUYA ET AL.	
	Examiner Ganapathy Krishnan	**Art Unit** 1623	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 11 July 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): 35 USC 112, second paragraph rejection of claims 1, 21-23 and 28.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,21-23 and 28*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see continuation sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623

Applicants have traversed the rejection under 35 USC 103 arguing that:
1. As shown in the Declaration of Mr. Nagatomo, Experiment 5 which corresponds to the method of Toshiyuki et al, produces high yield of a mono-glycoside compound. Experiment 4 in the said Declaration, which corresponds to the instant method produces high yileds of the diglycoside compound. The difference in the results in Experiments 4 and 5 is due to reaction temperature and concentration of acetic acid in the reaction system during the reaction.

2. Experiments 2 and 3 in the Declaration, which use conditions that are outside the scope of the instant invention produce mono glycoside as the main product.

3. According to applicants they have discovered that there is an equilibrium between the gallic acid methyl ester (starting material), mono-glycoside and diglycoside based on the concentration of the byproduct and acetic acid. Surprisingly the equilibrium will be shifted to produce the diglycoside when acetic acid has been removed. Toshiyuki does not teach or suggest the temperature range as instantly claimed and discloses a method for making the monoglycoside compound and not a diglycoside.

Applicants' arguments and the Declaration of Mr. Nagatomo have been considered but they are not found to be persuasive.

First of all, the product as instantly claimed is made by reacting gallic acid methyl ester with glucose pentaacetate. The first step in this reaction is the formation of the monoglycoside of gallic acid methyl ester and acetic acid (by-product). Now, inorder to form the diglycoside, the monoglycoside of gallic acid methyl ester should react with a second mole of glucosepentaacetate. This second step will also generate acetic acid as a by product. Since gallic acid methyl ester moiety in the monoglycosideproduct has two unreacted OH groups, these OH groups can react with the acetic acid generated to form the acylated monoglycoside. This would be a competing side reaction (leading to an unwanted product) in additiion to the reaction of the second mole of gucosepentaacetate to form the diglycoside (desired product). The reaction of acetic acid with the OH group of the gallic acid methyl ester moiety of the monoglycoside to give the unwanted by product is an esterification reaction (reaction between an acid and an alcohol). This is a fundamental reaction in organic chemistry that is well known to one of ordinary skill in the art. Inorder to prevent this unwanted side reaction from taking place in the system the skillled artisan knows that the acetic acid that is generated in the system should be removed as and when it is formed. The removal of acetic acid under reduced pressure is taught in the prior art of record in an analogous reaction (Toshiyuki, page 3, paragraph 9). Moreover, Toshiyuki (comparative example 1, page 4) teaches that an analogous reaction when performed at higher temperature gives low yields and also causes the browning of the product. So, one of ordinary skill in the art would want to remove the acetic acid and keep its concentration below 1.0 % or even less in order to suppress the unwanted reaction of the monoglcyoside with the acetic acid since this prevents the addition of a second glucose unit to the gallic acid part to form the diglycoside. Based on the teaching regarding the browning of the product and also low yields obtained, one of skill in the art would want to run the reaction at a lower temperature. Also it is well known to the skilled artisan that using reduced pressure will lower the boiling point of acetic acid and this will help remove it by distillation at a lower temperature as and when it is formed in the reaction system. The lower temperature will also avoid the browning of the product. It is well within the skill level of the artisan to adjust the temperature and pressure of the reaction to an optimal level such that the reaction proceeds at a reasonable rate and also the temperature at which the reaction is performed is high enough to distill the acetic acid out of the system without causing the browining of the product.

Applicants showing that Experiments 2 and 3 which use conditions outside the scope of the instant invention give the monoglycoside as the main product is also an expected result. In these two experiments the acetic acid is not removed. Since it is present in the reaction system it will react with the hydroxyl group of the gallic acid methylester monoglycoside to form the acylated derivative. Since this reaction consumes some of the gallic acid methylester monoglycoside, the amount of gallic acid methylester monoglycoside available to react with a second mole of glucose pentaacetate is reduced and hence the low yield of the diglycoside.

Therefore, applicants assertion that they have discovered that there is an equilibrium between the gallic acid methyl ester, mono glycoside and diglycoside based on the concentration of acetic acid by- product and that the removal of acetic acid under the conditions as instantly claimed, is not an unexpected discovery. It is a well known fact based on the type of reaction taking place. This is also well known to one of ordinary skill in the art and the skilled artisan will recognize all of this from the teaching of the prior art and his or her own general knowledge. Toshiyuki may not teach the formation of a diglycoside compound. But the skilled artisan knows that his teaching can be extended to the preparation of the diglycoside compound as instantly claimed since the chemistry is the same and requires the use of an excess of the glucose pentaacetate. There is a suggestion in the prior art that the instant method can be used to make the product of instant formula (3) with a reasonable expectation of success.